

Application No.: 10/565,446
Amendment and Response dated June 5, 2007
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REMARKS

Status of the Claims

Claims 1-18 are presently pending in the application. Cancellation of claim 18 has been requested herein.

Discussion of the Amendments to the Claims

The claims have been amended in an effort to point out more particularly and to claim more distinctly the subject matter of the present invention. In this regard, the claims have been amended in an effort to advance prosecution and not in acquiescence of any rejection. In particular, claim 1 has been amended with regard to the definitions of R1, R2, R3, R4, and R6, claim 2 has been amended with regard to the definition of R1 and R2, and claim 7 has been amended with regard to the definition of R6. Moreover, claim 1 has been amended to recite that the dehydrogenation catalyst is selected from compounds of the metals of Group VIII elements, and claim 14 has been amended to delete that recitation in view of the amendment to claim 1. Furthermore, claim 1 has been amended to recite the structural formula for Formula III. Claim 18 has been cancelled herein. No new matter has been added by way of the amendments to the claims.

Discussion of the Rejection of Claims 14 and 16 Under 35 U.S.C. § 112, First Paragraph

Claims 14 and 16 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. In particular, although the Examiner acknowledges that the specification is "enabling for the use of Pd catalysts," the Examiner nevertheless contends that "[t]he specification does not reasonably provide enablement for the exhaustive list of metals/complexes so claimed." (Office Action, page 2). Applicants respectfully traverse the rejection under 35 U.S.C. §112, first paragraph, for the reasons set forth below.

To comply with the enablement requirement, a disclosure must enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *See, e.g.*, M.P.E.P. §2164.01. In this regard, “[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. §112 is satisfied. *See* M.P.E.P. §2164.01(b) (internal citation omitted).

Applicants respectfully submit that the present specification provides ample guidance to enable one of ordinary skill in the art to make and use the subject invention using routine experimentation. For example, the method of the present invention is detailed in the specification at, for example, page 1, line 9 to page 4, line 10. With respect to step (B) of the method, suitable oxidizing agents are described at, for example, page 4, lines 13-24. With respect to step (A) of the method, the introduction of the protective group is described at, for example, page 8, line 14 to page 9, line 21. With respect to step (C), removal of protective groups is discussed, for example, at page 11, lines 16-25. Furthermore, with respect to all of steps (A) to (C), suitable organic solvents are described at, for example, page 11, line 26 to page 12, line 2, and suitable catalysts are described at, for example, page 10, lines 1 to 23. Furthermore, Applicants have provided several examples of the production of α,β -unsaturated compounds in accordance with the method of the present invention. In view of these disclosures, Applicants respectfully submit that one of ordinary skill in the art would be able to make and use the full scope of the claimed subject matter as set forth in claims 14 and 16 using routine experimentation.

With particular regard to the catalysts, Applicants respectfully submit that one of ordinary skill in the art would be able to use catalysts other than Pd using routine experimentation. Routine experimentation is, of course, not undue experimentation.

In support of the rejection, the Examiner alleges that selection of the catalyst is critical. However, this statement is unsubstantiated. In any event, as stated above, Applicants have provided ample guidance with respect to the catalyst at, for example, page 10, lines 1-23.

With respect to the reaction of the present invention, the Examiner alleges that “[w]hile applicant considers this reaction a dehydrogenation, it is better viewed as dehydrosilylation or in one case a dehydrocarbonylation.” (Office Action, page 3). In response, Applicants note that the starting material is a saturated compound and the resulting material is an unsaturated compound. Accordingly, the reaction is a dehydrogenation reaction. In any event, Applicants respectfully submit that whether the reaction is better named a dehydrosilylation or dhydrocarbonylation is irrelevant to the issue of enablement. Furthermore, in response to the Examiner’s comments at the top of page 3 of the Office Action, Applicants respectfully submit that the reaction mechanism involved is irrelevant and that the Examiner’s comments regarding Tsuji, *Tetrahedron Letters* 1984, 25, 4783 (which describes the combination of an oxidizing agent with a dehydrogenation catalyst for ester compounds) have no bearing on the enablement issue.

With particular regard to the Examiner’s comments regarding claim 16, Applicants respectfully submit that one of ordinary skill in the art would be able to make and use the subject matter of that claim using routine experimentation coupled with knowledge known to one of ordinary skill in the art. As such, Applicants respectfully submit that evidence that the additional complexing agent would stabilize the catalyst is not required. Indeed, it is well-established that compliance with the enablement requirement does not require exemplification of each and every embodiment of the present invention.

In view of the foregoing, Applicants respectfully submit that claims 14 and 16 comply with the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, Applicants

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respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, with respect to claims 14 and 16.

Discussion of the Rejection of Claims 1-17 Under 35 U.S.C. § 112, First Paragraph

Claims 1-17 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. In particular, the Examiner alleges that “[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.” (Office Action, page 3). Applicants respectfully traverse the rejection for the reasons set forth below.

For the reasons discussed above with respect to the rejection of claims 14 and 16, Applicants respectfully submit that the present specification provides ample guidance to enable one of ordinary skill in the art to make and use the subject invention using routine experimentation. Indeed, Applicants have not only described the method of the present invention in detail including suitable materials for use therewith, but have also specifically exemplified how to make α,β -unsaturated amide compounds in accordance with the present invention. Accordingly, Applicants respectfully submit that one of ordinary skill in the art would be able to make and use the full scope of the claimed subject matter using routine experimentation.

In support of the rejection, the Examiner, citing Bergmann et al., *Archive der Pharmazie (Weinheim)* 1986, 319, 203 and Thomas et al., *J. Chem. Soc. Perkin Trans. 1* 1989, 507, alleges that “amides are well known to undergo both N- or C- silylation as well as O-silylation and under the conditions given it has been shown that for certain substrates under the scope of the claims, C-silylation will occur.” (Office Action, page 3). In response, Applicants respectfully submit that whether or not the silyl compound can or would also undergo a C-silylation is irrelevant. At best, such a reaction would occur only to a minor extent, and the main reaction

would be the reaction with the reactive $-NH$ or $-OH$, as claimed in the present invention.

In support of the rejection, the Examiner relies on *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981). The facts of the *Howarth* case (and the *Ghiron* case cited therein), however, are distinguishable from the facts of the present application and have no bearing on the present application. One of ordinary skill in the art would know how to make compounds for use in the present inventive methods using routine experimentation coupled with information known in the art. Accordingly, it is respectfully submitted that the present application is fully enabling with regard to suitable starting materials. See M.P.E.P. §2164.01.

Furthermore, Applicants take exception to the Examiner's comments appearing on pages 4-6 of the Office Action. As discussed above, Applicants have more than exemplified how to achieve α,β -unsaturated amides in accordance with the present invention. Furthermore, with reference to "EP-A-0 478 366" which is cited in the Office Action at page 4, Applicants note that this patent document is not assigned on its face to Merck and does not contain the disclosure alleged by the Examiner. Rather, EP 0 478 366 pertains to recombinant hybrid immunoglobulin molecules.

In support of the rejection, the Examiner alleges that the present application has "few working examples." (Office Action, page 6). Applicants respectfully disagree. As discussed above, Applicants have provided several examples of the production of α,β -unsaturated amide compounds in accordance with the present invention. Moreover, a specification need not contain an example nor describe all actual embodiments to be enabling. See M.P.E.P. §2164.02. By providing several examples of the production of α,β -unsaturated amide compounds in accordance with the present invention as well as a detailed specification, Applicants have more than complied with the enablement requirement.

In view of the foregoing, Applicants respectfully submit that claims 1-17 comply with the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph, with respect to claims 1-17.

Discussion of the Rejection of Claim 1 under 35 U.S.C. §112, Second Paragraph, for Alleged Omission of Essential Structural Cooperative Relationships of Elements

Claim 1 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being incomplete for omitting essential structural cooperative relationships of elements. In particular, the Examiner alleges that "Formula III has been omitted from the claims and one would have difficulty ascertaining its structure." (Office Action, page 7).

Formula III. Claim 1 has been amended to recite the structure corresponding to Formula III. In view of the amendment to claim 1, Applicants respectfully submit that the basis for the rejection of claim 1 under 35 U.S.C. §112, second paragraph, is moot. Accordingly, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. §112, second paragraph.

Discussion of the Rejection of Claim 1 under 35 U.S.C. §112, Second Paragraph, for Alleged Indefiniteness

Claim 1 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner alleges that "[t]he group R8 is removed in every case in the instant invention and there is no case where it is an optional substituent, or optionally removed." (Office Action, page 7).

Applicants respectfully disagree with the rejection. As set forth in the specification, removal of protective group R8 is, in fact, optional (see, for example, page 4, lines 10-11, of the

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present specification).

In view of the foregoing and in view of the amendments to the claims herein, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. §112, second paragraph.

Discussion of the Provisional Non-Statutory Obviousness-Type Double Patenting Rejection

Claims 1-18 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly "being unpatentable over claim [sic] of copending Application No. 10/521,421." In response, Applicants respectfully request clarification of the claims of copending Application No. 10/521,421 to which the Examiner is referring.

Regarding U.S. Patent Application No. 10/521,421 (which was not published at the time of the filing date of the present application), that application specifically refers to a process for introducing a 1,2-double bond in 3-oxo-4-azasteroid compounds while the present patent application does not include 3-oxo-4-azasteroid compounds. As such, Applicants respectfully submit that the present application is both novel and non-obvious over U.S. Patent Application No. 10/521,421. Accordingly, Applicants respectfully request the withdrawal of the provisional non-statutory obviousness-type double patenting rejection. Furthermore, in view of the cancellation of claim 18, the basis for the rejection with regard to that claim is moot.

Discussion of the Rejection Under 35 U.S.C. §102(b)

Claim 18 stands rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 2,535,245 to Weisgerber et al. Applicants respectfully traverse the rejection for the reasons set forth below.

For a cited reference to anticipate a claim, that reference must disclose each and every limitation recited in that claim. Weisgerber, however, fails to disclose the method recited in

claim 1. Accordingly, it cannot be said that Weisgerber discloses a compound produced according to the method of claim 1 as required by original claim 18.

In any event, claim 18 has been cancelled in an effort to advance prosecution and not in acquiescence of the rejection. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(b).

Discussion of the Rejection Under 35 U.S.C. §103

Claims 1-17 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,084,574 to Bhattacharya et al. (hereinafter "Bhattacharya") in view of Minami et al., *Tetrahedron* 1986, 42 2971 (hereinafter "Minami") and Ito et al., *J. Org. Chem.* 1978, 43, 1011 (hereinafter "Ito"). Applicants respectfully traverse the rejection under 35 U.S.C. §103(a) for the reasons set forth below.

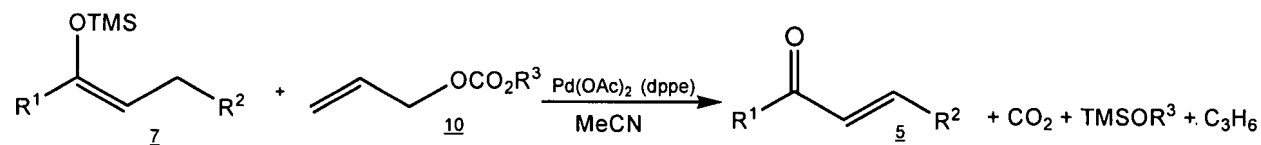
To establish a *prima facie* case of obviousness, the Examiner must establish that the cited combination of references disclose, teach or suggest every limitation of the claimed invention. Moreover, the Examiner must establish not only that there is some motivation to combine the teachings of the cited references, but also that there is a reasonable expectation of achieving the claimed invention upon doing so. *See* M.P.E.P. § 2142. The Examiner has failed to make this requisite showing.

The argument that the invention is not based on an inventive step involves two steps. Namely, in a first step, lactam compounds are considered as being chemically equal to ester compounds and, in a second step, it is then argued that the reaction of saturated ester compounds can simply be applied to amide compounds.

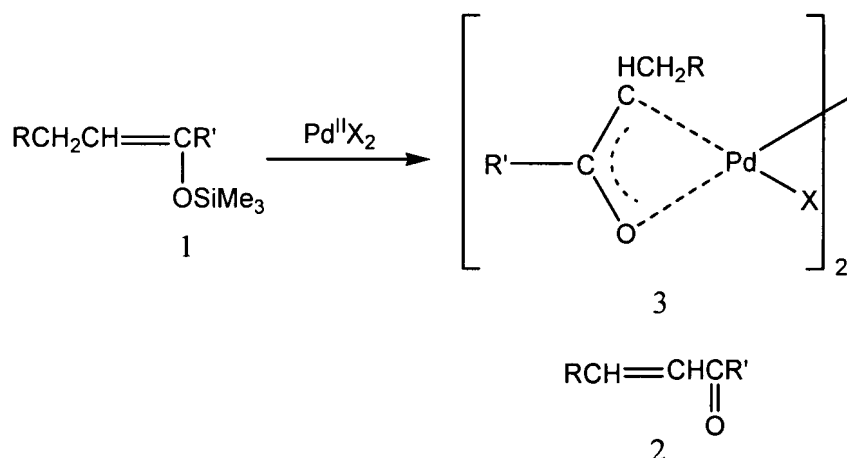
Lactam compounds and ester compounds are two different classes of compounds having different properties. The lactam group and the ester group have different polarities and yield entirely different chemical reactions, as is known to one of ordinary skill in the art. To combine the properties of these two classes of compounds in a general manner is simply not allowable. Lactam compounds are different from ester compounds and the reactions saturated ester compounds cannot simply be applied to amide compounds.

Bhattacharya discloses a method for the production of α,β -unsaturated lactams from the corresponding saturated lactams by reacting the saturated compound with a silylating and then with a quinone. The present invention differs from Bhattacharya (as far as a silylating agent on a quinone are used) in that a dehydrogenation catalyst is present. The use of a quinone with a dehydrogenation catalyst in combination with an amide is an essential feature of the invention and is novel and inventive over Bhattacharya. Accordingly, Bhattacharya fails to disclose, teach or suggest the present invention.

Furthermore, neither Minami nor Ito overcome the deficiencies of Bhattacharya. With particular regard to Minami, that reference discloses the following reaction scheme with respect to the generation of α,β -unsaturated carbonyl compounds:



Moreover, with particular regard to Ito, that reference discloses the introduction of an α,β carbon-carbon double bond to unsymmetrical ketones via the corresponding silyl enol ethers as shown below:



There is no disclosure, teaching or suggestion in either Minami or Ito, however, of a method as recited in the claims as originally presented or as amended herein.

With that said, Applicants respectfully disagree with the Examiner's characterizations of the disclosures of the Bhattacharya, Minami, and Ito references. Indeed, none of the references characterize their reactions as represented by the Examiner.

Absent any suggestion in Bhattacharya, Minami and Ito to combine those references, it is respectfully submitted that hindsight reconstruction is impermissibly being employed, using the subject application as a template to pick and choose portions of the cited references which, in turn, are being taken out of context. The use of such hindsight reconstruction in the absence of any suggestion to combine the references is, however, improper. *See, e.g., In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) (noting that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention"); *see also* M.P.E.P. §2145.

Thus, contrary to the Examiner's contention, it is Applicants' position that the Applicants' process is not an obvious variation of the work of Minami et al. and Ito et al.

Furthermore, with regard to Bhattacharya et al., *J. Am. Chem. Soc.* 1988, 110, 3318, that reference does not disclose, teach or suggest the present invention. Likewise, Applicants respectfully submit that the Examiner's comments with regard to Kawanaka et al. (*Bioorg. Med. Chem. Lett.* 2002, 12, 2291) are of no consequence. In particular, there is no disclosure, teaching or suggestion in Kawanaka of the present inventive method as recited in the claims as originally presented or as amended herein.

Applicants respectfully submit that the non-obviousness of the present invention is evidenced by the prior art itself. In particular, EP 0 298 652 (referring to amides) reportedly has a priority of June 29, 1987 and Tetrahedron Letters, Vol. 25, No. 42, 1984, pages 4783-4786 (Tsuji et al.) (describing the use of Pd-catalysts for making α,β -unsaturated esters) reportedly has an earlier publication date of 1984. Therefore, EP 0 298 652 could have described the use of Pd-catalysts for making α,β -unsaturated amides but EP 0 298 652 does not. This shows that esters and amides are different classes of compounds and that it is not obvious to use a method known for chemically reacting esters also for amides.

The priority date of the present application is more than 18 years from the publication date of Tetrahedron Letters, Vol. 25, No. 42, 1984, pages 4783-4786 (Tsuji et al.). Accordingly, it took more than eighteen years until the combination of the present invention was found, although it was known to use Pd-catalysts for making α,β -unsaturated esters. For the production of industrially important compounds such as α,β -unsaturated amides as claimed in the present invention, more than eighteen years is a very long time and shows that the present invention is based on an inventive step.

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Additionally, it should be noted that the process of the present invention gives unexpectedly high yields and product purities compared with EP 0 298 652.

As regards the case law cited in support of the obviousness rejection, Applicants respectfully submit that those cases are distinguishable on their facts from the case at hand and, as such, are not controlling. Furthermore, with regard to *In re Surrey*, 319 F.2d 233, 138 U.S.P.Q. 67 (CCPA 1963), that case has been overruled to the extent that it is inconsistent within *In re Magerlein*, 602 F.2d 366, 373, 202 U.S.P.Q. 473 (CCPA 1979).

In view of the foregoing, Applicants respectfully submit that the subject matter of the present claims (both as originally presented and as amended herein) is not obvious in view of the cited references. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103(a).

Additional Comments

None of the other prior art of record discloses, teaches or suggests the subject matter of the present invention.

Concluding Remarks

This application is believed to be in condition for allowance. Favorable action thereon is therefore respectfully solicited.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned at the telephone number given below.

The Commissioner is hereby authorized to charge payment of any additional fees associated with this communication, or credit any overpayment, to Deposit Account

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No. 08-2461. Such authorization includes authorization to charge fees for extensions of time, if any, under 37 C.F.R § 1.17 and also should be treated as a constructive petition for an extension of time in this reply or any future reply pursuant to 37 C.F.R. § 1.136.

Respectfully submitted,



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